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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/227,687	01/08/99	TALLY F	CPI98-03P9MA

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EXAMINER	
LEFFERS JR,G	
ART UNIT	**PAPER NUMBER**
1636	15

DATE MAILED: 03/13/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/227,687	Tally, et al.
Examiner	**Group Art Unit**
Gerald G. Leffers Jr.	1636

☒ Responsive to communication(s) filed on *Jan 2, 2001*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-66* is/are pending in the application.

Of the above, claim(s) *13-22, 28-49, 55, and 59-66* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-12, 23-27, 50-54, and 56-58* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *14 and 6*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Acknowledgment is made of applicants' submission of a paper copy of the sequence listing, corresponding CRF and attorney statement, filed 7/10/00. Applicants are hereby notified that the CRF comprised errors which were corrected by STIC prior to entry into the database (i.e. global insertion off hard returns in each amino acid sequence). Receipt is also acknowledged of applicants' Reply to the Restriction Requirement filed 01/02/01. Receipt is acknowledged of Information Disclosure Statements filed 12/1/99 and 1/19/01. The signed and initialed PTO 1449s for each have been mailed with this action.

Election/Restriction

Applicant's election without traverse of Group I (claims 1-12, 23-27, 50-54, 56-58) in Paper No. 13, filed 01/02/01, is acknowledged.

Drawings

This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed. Also, please note the attached PTO 948 mailed with this action.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 6-9, 11-12, 23-26, 50-53 and 56-58 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4-12 of copending Application No. 09/344,783. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reason.

The claims of the instant application are directed towards methods of identifying biomolecules which produce a phenotypic effect in a host cell (e.g. inhibiting infectivity of a pathogen) upon regulated expression of the biomolecule in the host cell following introduction of the recombinant host cell into an animal. The host cell can be a mammal or a pathogen. The biomolecule can be an RNA or a polypeptide. The claimed methods also include methods of screening for compounds which competitively bind to the same target component of the host cell as the biomolecule, with the assumption that such competitive binders will be candidate compounds for reproducing the observed phenotypic effect on the host cell in the animal as well.

The claims of the '783 application are drawn towards the same general methods as are claimed in the instant application, with the claims of the '783 application being drawn to specific embodiments encompassed by the broader claims of the instant application (i.e. pathogen host cells, the pathogen S.aureus and the biomolecular target methionyl-tRNA synthetase). Thus, the claims of the '783 application are totally encompassed by the claims of the instant application. If a patent resulting from the instant claims were issued and transferred to an assignee different from the assignee holding rights to a patent issued on the cited '783 claims, then two different assignees would hold a patent to the claimed methods of the '783 application. This would result, improperly, in possible harassment by multiple assignees.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12, 23-27, 50-54 and 56-58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-12, 23-27, 50-54 and 56-58 are vague and indefinite in that the metes and bounds of the terms "regulable" gene and "regulating expression" are unclear. The terms do not appear to be explicitly defined in the specification. In one sense, any gene operatively linked to a promoter sequence can be considered to be a "regulable" gene whose expression is regulated by the characteristics of that particular promoter (e.g. a cell-type specific promoter). In a more narrow sense, the terms encompass a gene under control of an inducible promoter such that the step of "regulating expression" comprises an active step by the practitioner to induce or inhibit expression of the gene (e.g. addition of an inducer). It appears from the specification that the latter example is what may be intended by the cited terms. It would be remedial to amend the claims to more clearly indicate the limitations intended by the use of the cited terms.

Claims 1 and 6 are vague and indefinite in that the metes and bounds of the phrase "monitoring said cell in the animal for a phenotypic effect" are unclear. The phrase is unclear because the process of monitoring the cells introduced into the animal for a phenotypic effect is described in different ways in the specification, including embodiments wherein it is the animal which is monitored for a phenotypic effect rather than the cell. For example, would monitoring an animal infected with a pathogen expressing a regulable biomolecule for signs of infection or even death constitute "monitoring said cell in the animal for a phenotypic effect"? It would be remedial to amend the claim language to more clearly indicate what limitation is intended by the cited phrase.

Claims 1 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: comparison to some sort of control wherein cells of the same type, but not expressing the biomolecule, are introduced into the same kind of animal and observed for phenotypic effect (e.g. cell phenotypes before and after induction of biomolecule expression). The claims are written such that a cell which manifests a phenotypic effect *necessarily* indicates the biomolecule is one that produces a phenotypic effect on the cell. Without this step one cannot assume that any phenotype observed is necessarily due to the expression of the biomolecule. It would be remedial to amend the claim language to include some sort of comparison step such that one can assume that an observed phenotypic effect is in fact due to the expression of the biomolecule in the cell.

Claims 7-8, 10-12, 56-58 are vague and indefinite in that the claims specify "suitable" control animals or cells. The term "suitable" is inherently indefinite in that the criteria for a "suitable" control is likely to vary from investigator to investigator. It would be remedial to amend the claim language to clearly indicate what exactly constitutes a "suitable" control for the recited methods.

Claim 7 is also vague and indefinite in that there is no clear and positive prior antecedent basis for the terms "fewer cells", "number of cells" and "growth of cells" in step (c) of the claim. It would be remedial to amend the terms to something like "fewer of the cells", "number of the cells" and "growth of the cells".

Similarly, claim 8 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term "of growth of cells" in step (d) of the claim. It would be remedial to amend the claim language to "inhibitor of growth of the cells".

Claim 11 is vague and indefinite in that the metes and bounds of the term "normal" growth are unclear. What exactly constitutes "normal" cell growth? Does the term refer to growth of a transformed cell in culture or within an animal? Does the term refer to growth of a pathogen in culture or in an animal host? It would be remedial to amend the claim language to more clearly indicate what is intended by the claim limitation of "normal" growth.

Claim 11 is vague and indefinite in that the phrase "..then the biomolecule is a biomolecular inhibitor of growth;" in step (d) implies that the biomolecule is necessarily an inhibitor of any kind of growth. It appears that the limitation is meant to specify that the biomolecule is actually an inhibitor of growth for the target cells. It would be remedial to amend the claim language to something like "..then the biomolecule is a biomolecular inhibitor of growth of the target cells;".

Claims 23 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a step wherein the effects of the compound on the cell with regard to the phenotypic effect are confirmed. The preamble specifies "A method for identifying a compound which produces a phenotypic effect..". The claim further comprises the limitation "whereby if the compound competitively binds to the target cell component, then the compound

produces the phenotypic effect...". A reasonable interpretation of the latter limitation is that if a compound binds competitively with a biomolecule to a target cell component, and wherein expression of the biomolecule has been shown to produce a phenotypic effect, the compound *necessarily* also produces the phenotypic effect. Such an assertion is contrary to what one of skill in the art would assume based on the steps of the claim as written and upon reading the specification. One of skill in the art would consider that a compound which is a competitive binder for the target cell component would only be a candidate for producing the phenotypic effect in the cell because of other factors which might interfere with the expected function of the test compound (e.g. clearing rapidly from the cell, stability of the compound within the cell, modification of the compound, etc.). The specification in fact teaches that such compounds can be considered to be drug *candidates* and that further testing can confirm that those compounds which bind competitively with the biomolecule actually possess the same effect with regard to phenotype of the target cells (page 32, lines 19-25). It would be remedial to amend the claim language to clearly indicate a step for confirmation of such phenotypic activity for a test compound or to indicate the method identifies *candidate* compounds which might exhibit the same phenotypic activity as the expressed biomolecule.

Claim 50 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term "the biomolecule" in step (d) of the claim. Claim 50 is also vague and indefinite in that the preamble of the claim specifies "A method for determining whether a biomolecule produces a phenotypic effect on a first cell..." and the claim concludes with

"..whereby, if a compound competes with the biomolecular binder for binding to the target cell component, then the compound produces the phenotypic effect on the first cell.". Upon reading the specification, it does not appear that the terms "biomolecule" and "compound" encompass the same scope. Thus, the end result of the claim does not match the preamble. Also, as indicated above for claim 23, there appears to be a missing step of confirming that a test compound has the same phenotypic effect on the target cell as the biomolecular binder.

Claims 56-58 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: infection of the control animals with the cells. Each of the claims specify a step of comparison of test animals with control animals yet there is no step specified for infecting the control animals with the pathogen.

Claims 56-57 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: confirmation that a test compound which binds competitively to a target cell component in a pathogen actually inhibits infection of a mammal by the pathogen. The rational for this rejection is the same as that given for claim 23 above.

Claim 57 is also vague and indefinite in that there is no clear and positive prior antecedent basis for the term "the control animals" in step (f).

Claim 58 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term "the control cells" in step (b). Claim 58 is also vague and indefinite in that the

preamble specifies "A method for identifying a biomolecular inhibitor of infection.." and the claim concludes with "..the biomolecule is a biomolecular inhibitor of cell growth.". It appears from following the steps of the claim that the conclusion should read something like "..the biomolecule is a biomolecular inhibitor of infection by the pathogen.".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-3, 4-6 are rejected under 35 U.S.C. 102(e) as being anticipated by Contag et al (U.S. Patent No. 5,650,135; see the entire document).

Contag et al teach methods and compositions for detecting and localizing light originating from a mammal wherein the light can originate from cells introduced into the mammal and wherein the emitted light can be used to generate animal models for disease states, to monitor the progression of disease or infection, and to screen putative therapeutic compounds effective to inhibit disease or pathogenic infection (Abstract). Contag et al teach that the cells of their

invention can be constructed to express a gene or genes encoding a luciferase tag which can be used to follow the status of the engineered cell following introduction into a mammal. Contag et al teach the light-emitting cells of their invention can comprise pathogens (e.g. Salmonella) or mammalian cells (e.g. tumor cells) (e.g. column 4, lines 30-48; column 5, lines 7-20). Contag et al teach that the promoters used in their methods to express the luciferase label can be inducible (e.g. tet, cytokine responsive, cell-type specific, etc) (e.g. column 14, lines 7-14). The patent teaches that a pathogen labeled by their methods can be used to study the infective process and to evaluate the effects of drugs or therapeutic agents on the infective process with a high level of temporal and spatial resolution (column 13, lines 30-36). Contag et al teach the engineered cells of their invention can comprise a construct wherein the gene encoding the light generating enzyme is linked with a therapeutic gene under control of a promoter such that light emission can be used to determine the location and level of expression of the therapeutic gene (column 12, lines 19-32).

Claims 1-4 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Kernodle et al (Infection and Immunity, January 1997, Vol. 65, No. 1, pp. 179-184; see the entire document).

Kernodle et al teach the targeted suppression of a toxin gene (hla) in S. aureus which results in reduced levels of the toxin in vitro and attenuated lethality in vivo. The authors constructed a mutated S. aureus comprising an antisense 600-bp fragment of the hla gene under

control of its own promoter (i.e. regulated expression of the RNA biomolecule) on an E.coli/S.aureus shuttle vector (Abstract). Intraperitoneal injection of mice with the antisense hla-containing transformant was significantly less lethal than in control mice injected with wildtype S.aureus or S. aureus comprising control plasmids (i.e. monitoring the cells in the animal for the phenotypic effect of toxin production) (Abstract; Figure 4).

Claims 1-6 are rejected under 35 U.S.C. 102(e) as being anticipated by Jacobs et al (U.S. Patent No. 5,981,182; see the entire document).

Jacobs et al teach novel vector constructs which can be used to identify novel open reading frames from various pathogenic organisms and which can be used to transform various host cells for use in vaccines (Abstract). The patent teaches that a preferred embodiment of the invention features the generation of a library of constructs, comprising a random library of genomic DNA sequences obtained from various pathogens (e.g. M. pulmonis, M. tuberculosis or M. bovis), which can then be screened to identify possible protective antigens (column 6, lines 39-47). The patent teaches that any number of suitable host cells can be transformed with the vector constructs of the invention and the transformed host cells utilized as expression or vaccine vehicles. Suitable host cells include, for example, M. tuberculosis or cultured mammalian cells (column 9, lines 5-33). The vector constructs of the invention are engineered to comprise a promoter to regulate expression of the gene encoding the putative antigen and can further have an inducible promoter to drive expression of the gene encoding the putative antigen (e.g. lac

operator/promoter in prokaryotic cells or metallothione promoter in eukaryotic host cells)(column 9, lines 45-64). The patent teaches a preferred embodiment wherein transformed M. bovis cells comprising a library of inserts encoding potential antigens are introduced into an animal as live carriers for the putative antigen, and following immunization/challenge, the protected animals are sacrificed in order to recover those sequences whose expression yielded protective immunity (i.e. monitoring the cell for a phenotypic effect) (column 9, lines 5-15).

Conclusion

No claims are allowed.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald Leffers, Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on Monday through Friday, from about 9:00 AM to about

5:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than 24 hours after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Rob Schwartzman, can be reached on (703) 308-7307.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

GL

G. Leffers, Jr.

Patent Examiner

Art Unit 1636

DAVID GUZO
PRIMARY EXAMINER

March 11, 2001